PHONOCARDIOGRAPHIC STUDIES OF THE SECOND HEART SOUND AND INDIRECT CAROTID PULSE WAVE STUDIES IN OBSTRUCTION TO LEFT VENTRICULAR OUTFLOW

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Phonocardiographic Studies of the Second Heart Sound and Indirect Carotid Pulse Wave Studies in Obstruction to Left Ventricular Outflow

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INTRODUCTION

It is commonly accepted by clinicians that one sign of obstruction to left ventricular outflow--such as that which occurs in aortic stenosis--is paradoxical splitting of the aortic and pulmonic components of the second heart sound (Tavel, Levine and Harvey, Luisada, Butterworth). The mechanism which is proposed to explain this phenomenon is that obstruction causes a delay in left ventricular ejection of blood. The result of this is a prolongation of left ventricular systole and a consequent delay of aortic valve closure. The normal hemodynamics of the right side of the heart are relatively unaffected, and the pulmonic valve closes at the normal time. In paradoxical splitting the aortic valve is so delayed that it closes after the pulmonic--a reversal of the normal sequence. A stenotic valve must be severely obstructive before this reversal of events occurs, usually attaining a systolic pressure difference across the valve of more than 75 mm. of mercury (Braunwald, Roberts et al.).

Aortic stenosis, however, is seen in a full spectrum of severity. It is reasonable to expect, therefore, that in milder cases of obstruction a lesser delay in aortic valve closure must occur--a delay which is insufficient to place the aortic component after the pulmonic component in time. This "pre-paradoxical splitting" situation is widely observed clinically. It is heard as

"narrow" splitting when aortic closure is slightly delayed and as a "single" second sound when it is delayed sufficiently to occur simultaneously with the pulmonic component. A logical conclusion would be, therefore, that the magnitude of delay of aortic closure should correlate with the degree of obstruction, or at least yield some information with regard to the physiology of the lesion. The literature shows that these correlations have been attempted--but only in studies of patients with relatively severe disease of long duration. Cases with lesser degrees of obstruction and of shorter duration such as commonly occur in the pediatric population have been largely overlooked. Yet it is this population which should provide the clearest information with regard to the patho-physiology of obstruction to left-sided outflow, before long-standing disease has introduced complicating factors.

It is the purpose of this study to investigate the behavior of the aortic and pulmonic components composing the second heart sound in response to obstruction of left-sided outflow, and to determine if various measurements of systolic ejection can serve as indicators of the degree of obstruction.

Two parameters will be utilized: phonocardiographic recordings of the second heart sound and indirect arterial pulse wave tracings from the carotid artery. The use of these parameters is widely accepted in this field and their significance amply documented in the literature.

REVIEW OF THE LITERATURE

Phonocardiographic studies of the second heart sound have been extensively utilized in the past. Their value lies in the fact that each component, when correlated with other parameters and properly interpreted, serves as a meaningful indicator of the hemodynamics occuring in its respective side of the heart.

In 1832 Rouanet wrote that the second heart sound resulted from closure of semi-lunar valves. Potain in 1865 made the clinical observations that the second heart sound, when auscultated over the pulmonic area in certain patients, was split and that in these patients the degree of splitting varied with respiration. Katz in 1925 explained this split physiologically by timing the cardiac cycle in both sides of the heart in laboratory animals and noting the asynchronous manner in which the two semi-lunar valves closed. Leatham and Towers, and Leatham (1954), in clinical studies, demonstrated by taking synchronous phonocardiograms from the different auscultatory areas, that the phonocardiographic representation of splitting of the first and second components of the second sound was due to closure of the aortic and pulmonic vlaves respectively. Luisada (1965) challenged the concept that valve closure itself is responsible for the aortic and pulmonic components of the second sound, but agrees that the timing of each sound is mainly determined by closure of these valves in conjunction

with the reversal of flow of the blood column and the resultant vibration of vessel walls and other transmitting structures.

There has also been controversy over the exact nature of normal physiologic splitting and the inspiratory augmentation of this splitting. Leatham and Towers studied ten children and ten adults in 1951, determining normal and abnormal splitting of the second heart sound during inspiration and expiration. They documented the inspiratory increase in splitting and hypothesized that augmentation was solely the result of delay in pulmonic closure. Boyer and Chisolm, reporting on a study of twenty children, challenged this concept, stating that the movement toward an earlier temporal position of the aortic component contributed equally to inspiratory augmentation. Shafter confirmed Boyer's and Chisolm's views but disagreed with the relative importance of the movement of the aortic component. Subsequent reports by Castle and Jones, Aygen and Braunwald, and Shah and Stodki have all differed slightly in attaching relative significance to each component's contribution to the resultant respiratory variation of splitting.

During the past two decades, nearly every type of cardiac anomaly and dysfunction has been investigated in terms of its effect on the components of the second heart sound as determined by phonocardiography. In 1952, Brigden and Leatham applied phonocardiographic techniques to the study of the second sound in mitral insufficiency. In 1956, in collaboration with Gray, Leatham documented the fixed wide splitting commonly heard in the presence of atrial septal defects. This topic was explored further by

Wood, and later by Aygen and Braunwald. Jonsson investigated the affects of pulmonary hypertension on the pulmonic component. Leatham and Weitzman, Vogelpoel and Shrire, Aygen and Braunwald, and Gamboa all investigated pulmonic stenosis and discovered positive correlations between increased right-sided ventricular pressure secondary to pulmonic stenosis and delay in pulmonic closure. Van der Hauwert and Nadas, Leatham and Segal, and Hollman et al. found that ventricular septal defect resulted in widened splitting. A partial explanation for this phenomenon was thought to be that the increased volume load on the right heart resulted in prolonged ejection time and a resultant delay in the pulmonic component. Other factors, including early closure of the aortic valve due to the double outflow from the left ventricle are perhaps as important. Shah and Stodki studied the effects of systemic hypertension on the second heart sound.

The relevance of these investigations to the present study lies in the general laws which can be inferred from them; namely, that the two chief factors causing prolonged ejection and delayed aortic or pulmonic components (in the absence of conduction defects) are increased volume load or increased pressure load to the ventricles. Further, it has been shown that each ventricle acts somewhat independently of the other, responding to any pathology present in its side of the heart and affecting the closure of its own semi-lunar valve.

Only a few studies have dealt directly with aortic stenosis. By analogy to the situation in pulmonic stenosis, it was

expected that correlations could be found between degree of aortic obstruction and the delay in aortic closure or the decreased splitting of the second heart sound. Braunwald, Goldblatt, et al. reported prolonged total ejection time and delay in aortic closure in all types of aortic stenosis. Gray noted the presence of paradoxical splitting in fifty per cent of those patients with known severe aortic stenosis. Aygen and Braunwald reported prolonged total ejection time, decreased splitting, and decreased inspiratory augmentation of the splitting in congenital aortic stenosis. Only rough correlations could be made between the degree of obstruction and these findings. Gamboa was unable to find significant changes in a group of patients with aortic stenosis. All of these studies utilized subjects with relatively severe aortic stenosis. The groups of subjects studied were composed at least partly of adult populations. Therefore, many subjects had long-standing disease; it is likely that some had complicating factors such as myocardial ischemia or conduction defects.

One of the most thoroughly investigated parameters used in studying obstruction to the left ventricle and the prolongation of ejection, which is believed to occur secondary to obstruction, has been the indirect arterial pulse wave. Using various electrical (and earlier--mechanical) devices on the surface of the body, one can detect instantaneous small volume changes within the segment of major artery beneath the sensing device. Due to the nature of arterial walls and the intervening tissues, there exists an approximately linear relationship between the externally recorded volume changes and the internally occurring pressure

changes. Further, it has been demonstrated that the indirect pulse tracing taken from the carotid reliably reflects the pressure changes of the aorta (Robinson, 1963-II; Weissler et al., 1961). The indirect carotid pressure pulse, therefore, serves as a good physiologic measure of the mechanism of systolic ejection.

The history of the development of the use of arterial pulse wave recordings in the study of left-sided obstruction is a long one. Marey, in 1863, was the first investigator to utilize graphic methods of recording pulse waves. He noted subjective differences between the waves produced by subjects with aortic insufficiency and aortic stenosis (cited in Epstein and Coulshed). In 1904 Bowen utilized tracings taken from the carotid artery to measure the duration of left ventricular ejection (cited in Epstein and Coulshed). Lombard and Cope observed that the duration of left ventricular systole is influenced by sex and the phase of respiration and that an inverse relationship exists between heart rate and ejection time in the normal population (Lombard and Cope). Katz and Feil in 1925, using improved optical equipment, demonstrated prolonged systolic ejection times in a clinical population with aortic stenosis (Katz and Feil). In the following year they demonstrated that the peripheral pulse reliably reflects central (aortic) events (Feil and Katz). Their clinical observations mentioned above were verified by producing an experimental model of stenosis and noting that this too produced a prolonged ejection time as detected by central aortic pressure pulse recordings. They noted changes in the

pulse wave, including decreased amplitude, prolonged gradiant of ascent, decreased depth of dicrotic incisure, and superimposition of systolic vaibrations and an anacrotic notch; Katz also found that the increase in ejection time was related to the degree of stenosis (Katz et al., 1928). Over several decades Wiggers and several other investigators performed many experiments on laboratory animals, simulating both aortic stenosis and coarctation of the aorta. They recorded both central pressure and indirect pulse waves from these laboratory preparations, and documented the degree of obstruction necessary for phonocardiographic and physiologic changes to occur. Wiggers noted the changes produced in pulse wave morphology by obstruction, and the differences between ventricular, aortic and peripheral waves in the manner in which they reflected the degree of obstruction (Wiggers, 1949, 1952, 1952). Weissler et al., (1961) verified the close agreement between measurement of ejection time obtained by intra-aortic pressure pulse studies and indirect carotid pulse studies. Hamilton, Benchimol et al. (1960), and Salans et al. also compared central and peripheral arterial pulses.

During the past ten to twenty years many investigators have applied the technique of indirect arterial pulse wave recording to the clinical study of left-sided obstructive disease -- especially aortic stenosis. Recordings were taken at first largely from the brachial artery, but these proved to be less satisfactory than carotid tracings, since brachial tracings were incapable of showing significant distinguishing alterations from the normal (Goldberg et al., Gorlin and Case, Hancock and

Abelman, Hancock and Fleming, Robinson, Wood). The majority of studies based on carotid tracings showed that certain alterations in the morphology of the indirect pulse wave were commonly seen in subjects with aortic stenosis (Daoud et al., Donoso, Duchosal, Epstein and Coulshed, Grishman et al., Hamilton, Robinson-I., Smith et al.): slow, flattened upstroke and late peak of decreased magnitude, an anacrotic notch in the first two-thirds of the upstroke, vibrations or "carotid shudder" along the peak of the pulse, and in certain cases flattening of the dicrotic notch or incisure.

In an attempt to objectively measure these subjective variables the total systolic ejection time was measured, as was the period of pressure rise called the upstroke or u-time, and the t-time, representing the period of early outflow during which the upstroke reached the first half of its ultimate height (see Figure 1) (Benchimol et al., 1960; Braunwald, Roberts et al., 1963; Daoud; Donoso; Duchosal; Eggink et al.; Epstein and Coulshed; Robinson--I). In general the investigators found that prolonged ejection times and retarded ejection during the earlier part of systole (prolonged u-times and t-times) were indicative of the presence of aortic stenosis, although the diagnosis of severe aortic stenosis could not be excluded by the absence of these prolonged intervals. Donoso et al., and Eggink et al. did not attempt to correlate their findings with the degree of stenosis. Other authors who did attempt to make this correlation were not able to obtain satisfactory criteria based

on these variables which were capable of predicting the degree of severity of the stenosis. Combinations of abnormal values for these variables would suggest the presence, but not the degree, of obstruction (Epstein and Coulshed, Robinson--I., Benchimol et al. 1960, Daoud et al.). Attempts were made to refine the techniques by employing other measurements obtainable from the pulse tracing. Eggink et al., and Coulshed and Epstein studied the ascending index (upstroke time/ejection time), but found a large degree of overlap with the normal population. Benchimol et al., 1960 and Daoud et al. studied the "ejection angle" formed by the intersection of a vertical line with the upstroke of the pulse, and other workers (Daoud et al.) utilized other angles formed by the pulse tracing. The fact that these angles were largely determined by non-standardized amplification of the particular equipment used negated the reproducability of their results, and therefore the value of these techniques.

It is surprising that this correlation between severity of stenosis and prolonged ejection and upstroke times which was made experimentally (Katz et al., 1928) cannot be borne out clinically. Among the factors which must be considered, in addition to severity, is the period of time during which the subject has tolerated the lesion. Among the studies noted above, the age of the patients as well as the duration of their lesions varied widely. Many of the subjects had long-standing disease of several decades. Only Eggink et al. considered the duration of the lesion by selecting a pediatric population.

Another reason for the lack of correlation may be that most

of the above-mentioned authors failed to consider the effect of heart rate upon the ejection time. Only Benchimol et al., 1960, and Epstein and Coulshed utilized the Bazett formula in order to simulate comparable heart rates in all the subjects studied.

It was hoped that by taking into account these last two factors in the present work, more information would be obtained from the study of the indirect carotid pressure pulse, perhaps leading to diagnostic criteria of the severity of the stenosis. The population studied was from five to twenty-one years of age representing grades of obstruction from very mild to severe. All results were interpreted after utilizing the Bazett formula to standardize the heart rate. Further, the carotid pulse wave studies were utilized to clarify the findings obtained in the phonocardiographic studies in the same population. Since the latter studies revealed prolonged total systolic time (from the onset of myocardial excitation to the end of the mechanical systole represented by valve closure), it was felt that carotid pulse studies would also yield information regarding the lengthened systole seen in left-sided obstruction; specifically, whether or not it represented a purely mechanical phenomenon.

MATERIALS AND METHODS

I. Population

A control series of thirty healthy children--fifteen male and fifteen female subjects between the ages of five and sixteen years--were studied. They were taken from among patients entering the General Pediatric Clinic of the Yale-New Haven Hospital during the summer of 1967. They were selected only on the basis of negative medical histories and absence of positive findings on physical examination. The reason for attending clinic in most cases was the need for school or camp physical examination or follow-up examination after acute non-cardiovascular illness. Roentgen and electrocardiographic studies were seldom available to corroborate the assumption that these subjects had normal cardiovascular systems, since in this age group such studies are infrequently done on normal, healthy children. The method and purpose of the experiment was explained beforehand to the responsible adult when that person was present. No subject refused to take part in the study. Only one subject from among thirty-one children consecutively tested had to be excluded from the study on the basis of poor technical quality of the tracing. The experimental results from this group were used to formulate the standards of normal cardiovascular systems with which the pathologic population could be compared. The experimental results obtained from this group, when compared with those in the literature,

also served to verify the reliability of the techniques used in this study by this investigator.

Thirty-four youngsters with various types of obstruction to left ventricular ejection of a congenital nature were studied in a consecutive manner as they entered the Yale-New Haven Hospital or Pediatric Cardiology Clinic between May, 1967 and February, 1968. Every subject who entered the clinic and was asked to cooperate with the study did so. Included in this population of thirty-four subjects were twenty children in whom the firm "clinical" diagnosis of obstruction to left ventricular ejection had been made, but who had not had catheterization or angiographic studies to document and quantify their lesion. Nineteen of these were suspected of having predominantly aortic valvular stenosis of some discrete type, and one was diagnosed as suffering from coarctation of the aorta. All the lesions represented by this group were judged to be mild by clinical, electrocardiogrphic and roentgenographic criteria. According to their histories, these patients were asymptomatic.

The remainder of the pathologic population were children in whom the lesions were well-documented by catheterization and angiographic studies. Eight had pure valvular aortic stenosis. There were five subjects with double lesions: the predominate lesion was aortic stenosis, coexisting with minimal aortic insufficiency. There was one case of coarctation of the aorta. It was possible to group these patients into three categories on the basis of the catheterization data: mild (0-30 mm. Hg pressure difference across the obstruction); moderate (31-60 mm. Hg); and severe (61 or more mm. Hg). There were no known cases of hypertrophic sub-aortic stenosis. There are other

known causes of paradoxical splitting, including conduction defects (Gray, Haber and Leatham), patent ductus (Gray), ischemic heart disease (Dickerson and Nelson, Yarchak and Gorlin), and Wolff-Parkinson-White syndrome (March et al., Zuberbuhler and Bauersfield). None of the subjects studied were known to suffer from any of these anomalies or dysfunctions.

All catheterization studies were done in, and interpreted by staff of the Yale-New Haven Hospital. None of the subjects was felt to be in failure during any of the studies.

II. Equipment and Methods

This study required the use of the "Sanborn Polybeam" four-channel photographic recorder, "Twinbeam oscilloscope" and four appropriately matched Sanborn amplifiers: an electrocardiographic amplifier; an audio (phonocardiographic) amplifier; a high gain amplifier (for carotid tracings); and a low gain amplifier (for plethysmographic tracings). The above equipment was all housed soon after the study was begun in a separate sound-proofed examining room convenient to the pediatric clinics.

Electrocardiographic (Lead II), plethysmographic (respiratory variations in external chest diameter), phonocardiographic, and indirect pressure pulse wave (carotid artery) data were all recorded continuously and simultaneously on photographic paper. The electrocardiogram served as an independent timing reference for the beginning or each cardiac cycle and as a measure of the heart rate and presence of any arrhythmias. The external carotid pulse tracings were utilized

to investigate various physiologic measures of systolic ejection. They also provided a reference point (dicrotic notch) by which the aortic component could be distinguished from the pulmonic component of the second heart sound according to the method described below. The plethysmographic tracing documented the rate and phases of the respiratory cycle. The phonocardiogram permitted the study of the second heart sound and its components. The indirect carotid pressure pulse was taken at the bifurcation of the right carotid artery in nearly every case, by a crystal microphone held in place with minimal pressure by a rubber strap. The plethysmographic mercury strain gauge was placed around the thorax from the sternum to the scapula. The gauge itself produced negligible pressure on the chest while maximally recording changes in anterior-posterior diameter.

The phonocardiograms were recorded by means of a dynamic microphone serially placed, at least briefly, at each of the major auscultatory areas. As reported by Sainani and Luisada, and Leatham, 1958, the most useful tracings were recorded over the second and third left parasternal areas where the pulmonic component was optimally transmitted, although on a few occasions the best location was found to be further to the left in the second and third intercostal spaces. This methodical recording from the entire precordium insured against producing unsatisfactory tracings when a subject had a minimally audible pulmonic component. The phonocardiographic tracings were recorded at paper speeds of either 75 or 100 millimeters per second in order to assure an accuracy of ± 0.003 seconds (Tavel).*

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* That is, individual intervals were measured with an accuracy of ± 0.003 seconds. The results are frequently reported in the text and graphs to .001 second. These represent averages or approximations and do not indicate accuracy of this degree with the methods used.

Audiofiltration as described in the literautre (Rappaport and Sprague, 1941, 1942; Williams and Dodge; Tavel; Sainani) was utilized, permitting high-frequency cut-off above either 100 or 200 cycles per second, with a cut-off slope of twelve decibels per octave. In most cases measurements were taken from those tracings which were filtered at 200 c.p.s., but in a few subjects it proved to be easier to use those phonocardiograms which were recorded with a 100 c.p.s. cut-off.

Each subject, after being connected to the various recording devices, was allowed a reasonable period of time in which to achieve a steady state. All recordings were done with the patient in a supine position and breathing spontaneously. The neck was slightly extended and the head turned a little to one side in most instances, although with a few subjects it was necessary to use a six-inch roll placed under the neck in order to facilitate a technically adequate carotid tracing. It was felt that this position and state most nearly approximated that of the typical physical examination. It also minimized positional and functional variables which are known to influence the second heart sound (Castle et al.; Shafter; Leatham, 1958; Levine and Harvey; Mason et al.). Enough film was exposed to permit the recording of all four parameters during a minimum of at least three respiratory cycles (three to five cardiac cycles) at each filtration level. The above technique, once mastered, permitted technically satisfactory tracings of all four parameters in all but one, restless patient.

From the phonocardiographic tracings obtained in this manner the following measurements were made during both phases of the respiratory cycle: 1) the R-R interval, or cardiac cycle length, derived from the electrocardiographic QRS complexes; 2) the Q-II_A interval*, measured

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* The Q-II_A interval is the sum of the time required for electrical excitation and isovolumic contraction plus the time required for ejection (onset of the pressure rise to aortic valve closure).

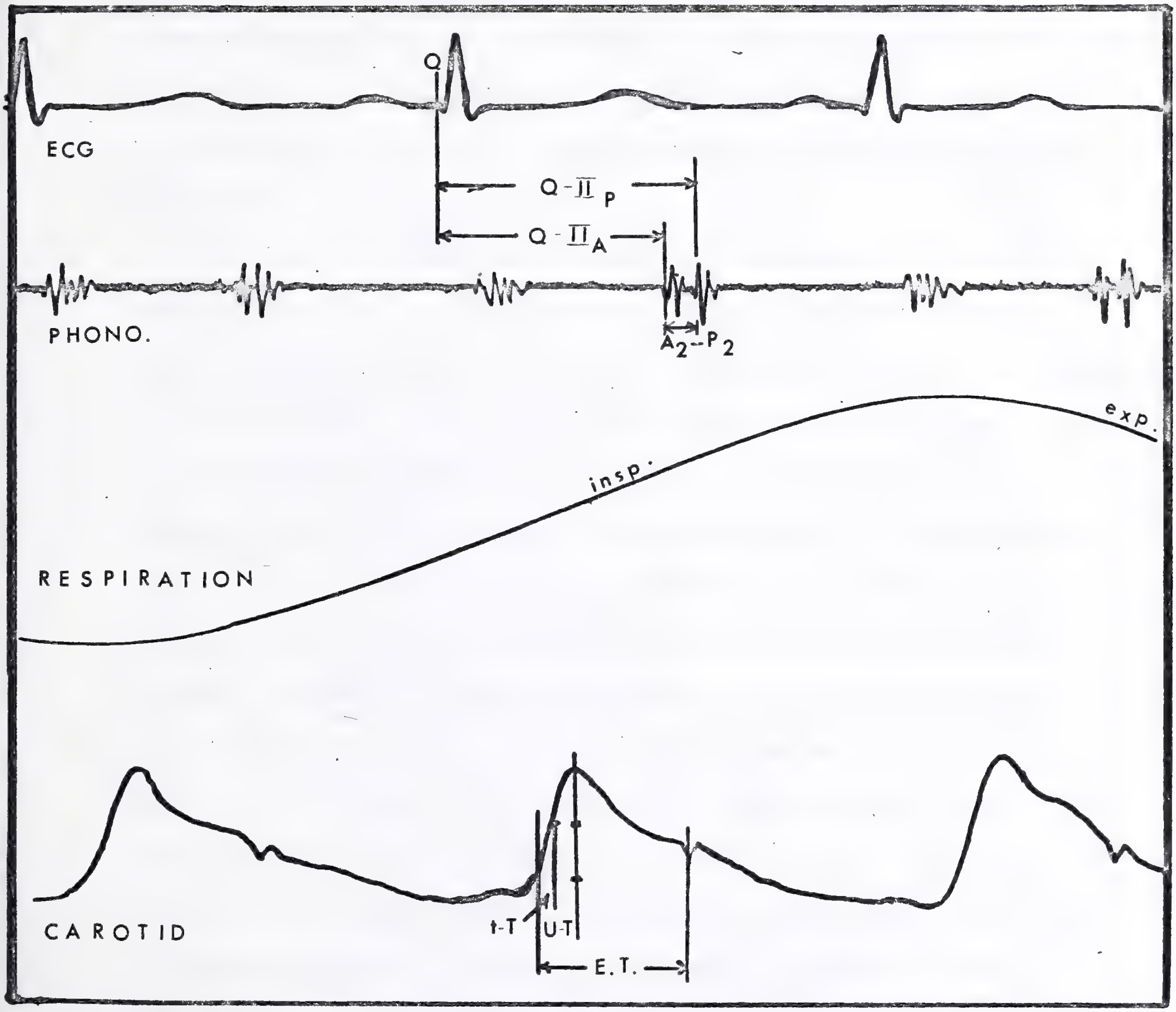


FIGURE 1

Figure 1: A typical tracing. Time lines and amplitude markings have been removed to show more clearly the method of measuring the intervals used in this study. Note that it is possible to record all four parameters simultaneously.

from the onset of the electrocardiographic QRS complex to the first peak registering the aortic component of the second heart sound in the phonocardiogram (Aygen and Braunwald); 3) the Q-II_P interval, similarly measured from the QRS complex to the pulmonic component; and 4) the A_2 to dicrotic notch interval. These measurements are shown graphically in figure 1.

From the first three measurements the following could be arithmetically computed: 1) the heart rate (R-R x 60); 2) the A_2-P_2 interval (Q-II_A subtracted from Q-II_P), which represents the "splitting" of the second heart sound; and 3) the inspiratory augmentation of the A_2-P_2 interval (inspiratory A_2-P_2 minus expiratory A_2-P_2). The A_2 - dicrotic notch interval provided a reliable method of distinguishing aortic from pulmonic components of the second heart sound. This was possible because the notch, which is caused by aortic valve closure, maintains a constant temporal relationship to the aortic component, i.e., the period it takes for the impulse to travel along the blood column. The velocity of transmission varies from person to person, but remains constant in any given individual. The pulmonic component, however, bears no such constant relationship to the notch. In fact, the length of time by which the P_2 precedes or follows the notch varies widely. The A_2 -dicrotic notch interval was measured initially at the apex where the pulmonic component is absent or minimal. The interval could then be applied to sounds recorded elsewhere on the precordium, clarifying the component parts of any second heart sound.

The values which were finally reported for these variables for the purposes of this study were those representing the cardiac cycles having the maximal intervals between aortic and pulmonic sounds in

inspiration, and the cardiac cycles having minimal intervals between these components in expiration. These extremes of maximal and minimal splitting may have occurred in the same respiratory cycle or as much as two or three respiratory cycles apart, depending on the rate and depth or respiration. The maximal inspiratory A_2-P_2 and minimal expiratory A_2-P_2 were nearly always found to occur at the peaks of inspirations and expirations respectively.

The carotid tracings were analyzed in terms of three variables: 1) the total ejection time (the time required for the left ventricle to eject its contents), measured from the initial steep rise of the upstroke marking the onset of ejection to the dicrotic notch marking closure of the aortic valve (Benchimol et al., Tavel); 2) the upstroke or u-time, measured from the beginning of the ascending limb to the peak of the pulse wave (Benchimol et al., Tavel); 3) the t-time, measured by computing the time necessary for the upstroke to achieve one half of its ultimate height (Duchosal et al.; Benchimol et al.; Tavel). See figure 1. The reported measurements represent the mean values of measurements made during one complete respiratory cycle (three to five cardiac cycles).

All measurements were corrected for heart rate by the Bazett formula; that is, by dividing the length of each interval obtained in the carotid pulse or phonocardiographic tracing by the square root of the R-R interval (Tavel). While other correction formulae are found in the literature (Weissler et al., 1963), none of these have been verified for aortic stenosis or coarctation of the aorta. This particular formula corrects intervals found at other heart rates to values which would be found if the rate were sixty cardiac cycles per minute,

thereby making possible comparisons between subjects.

All data obtained in this study were subjected to standard statistical analysis: mean values, distribution curves, standard errors and deviations, t-test and significance were all calculated according to methods described in Hill, and Bailey.

RESULTS

I. Phonocardiographic Studies

A. Normal Subjects (Control Population)

The interval Q-II_A was measured during spontaneous expiration and inspiration in thirty normal subjects. Distribution curves of the rate-corrected values (Figures 2a and 2b) show approximately Gaussian distributions. The rate-corrected mean Q-II_A during inspiration is 0.422 seconds, while the mean Q-II_A during expiration is 0.430 seconds. These values with their respective standard errors and standard deviations are entered in Table 1.

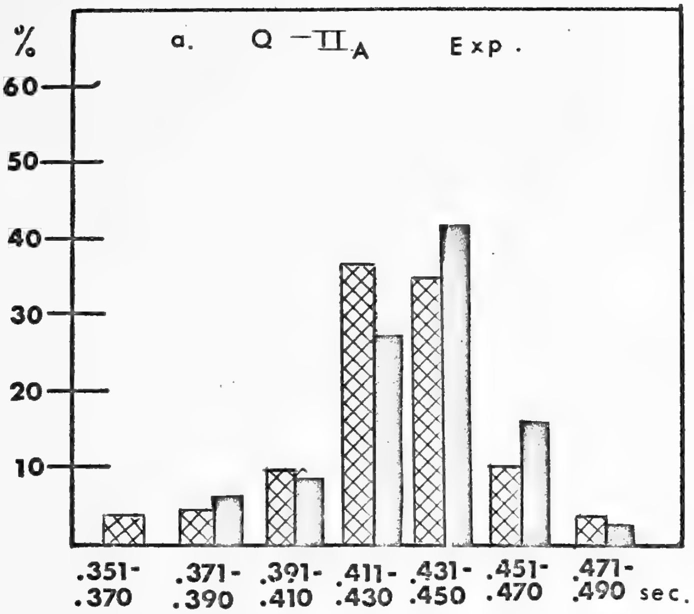
TABLE 1

Expiratory Q-II_A	Inspiratory Q-II_A	Expiratory A_2-P_2	Inspiratory A_2-P_2	Inspiratory Augmentation of A_2-P_2
0.430 ± .012 SE = ± .002	0.422 ± .021 SE = ± .004	0.025 ± .011 SE = ± .002	0.053 ± .021 SE = ± .004	0.028 ± .010 SE = ± .002

Table 1: Mean values for phonocardiographic data obtained in this study of thirty normal subjects. Note that ± represents the standard deviation of the population of normals sampled. S.E. means standard error which, if multiplied by 2 gives the approximate confidence limits for the true mean of the population sampled with p less than .05.

The interval, or "splitting", between the aortic and pulmonic components (A_2-P_2) of the second heart sound during inspiration and

FIGURE 2



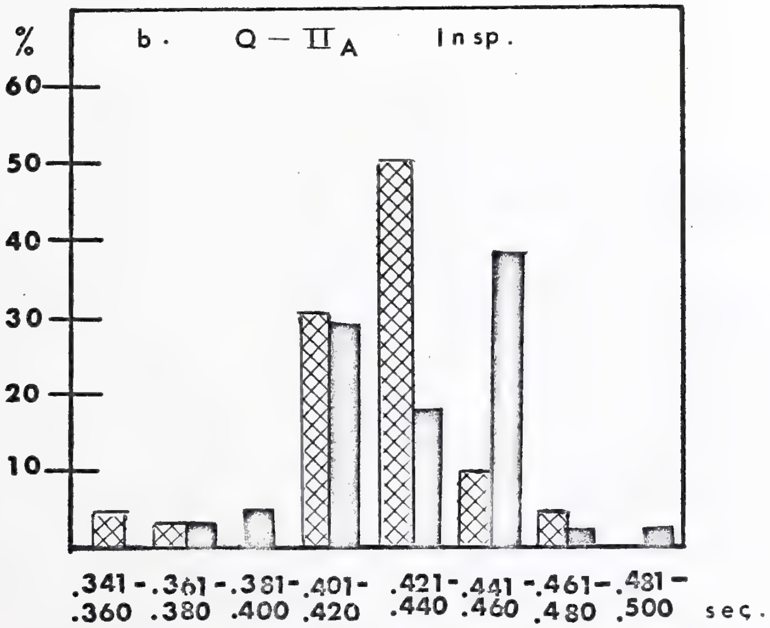


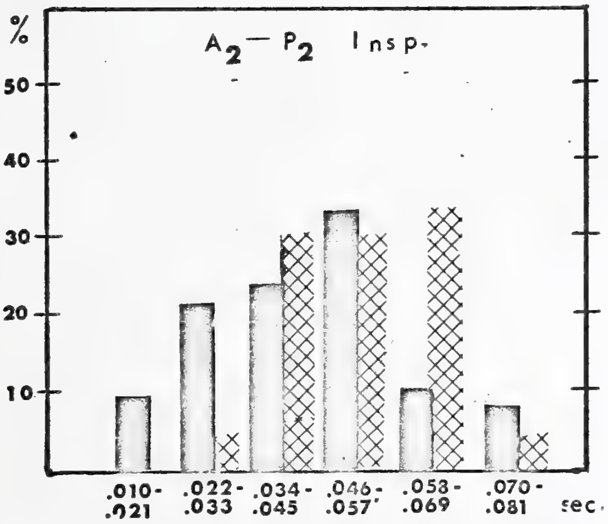
Figure 2a,b: Distribution curves for the rate-corrected values found for Q-II_A during inspiration and expiration. Solid lines represent population with obstructive pathology, while cross-hatched lines represent normal population. Note the approximately Gaussian distribution in the normal population and the somewhat skewed distribution present in the population with pathology.

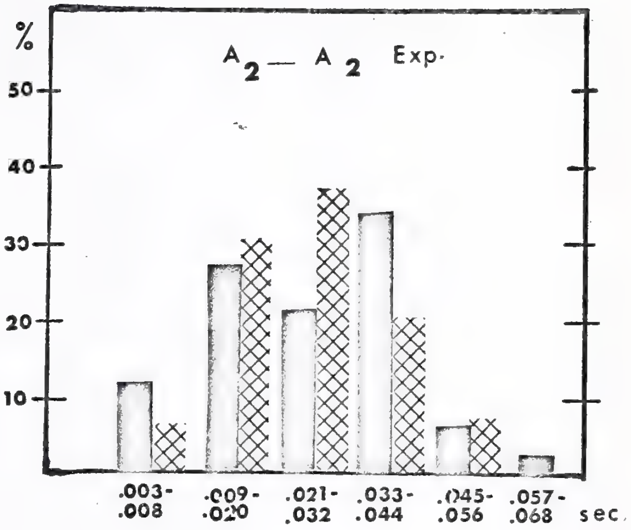
during expiration was computed for each subject. The difference between inspiratory and expiratory A_2-P_2, representing the inspiratory augmentation or variation of the split second sound, was also computed. Rate-corrected values were subjected to statistical analysis and are represented in Table 1. The mean expiratory A_2-P_2 was 0.025 seconds, and the mean inspiratory A_2-P_2 was 0.053 seconds. Therefore, the inspiratory augmentation of the split second heart sound was 0.028 seconds. There was detectable splitting and respiratory variation of splitting in every normal subject tested. Distribution curves of these measurements again show approximately normal curves about their mean values (Figures 3a, 3b, 3c).

It can be seen that in normal subjects A_2-P_2 varies with respiration--increasing in inspiration and decreasing in expiration--a well-known observation to clinicians. It is less easily observed clinically that this respiratory variation of A_2-P_2 is composed of two unequal contributing factors: the lesser is the temporal movement of A_2 and the greater is the movement of P_2. The former was measured directly (see Table 1); the latter can easily be calculated by adding the inspiratory and expiratory A_2-P_2 intervals to their respective Q-II_A intervals. A graphic representation of the normal second heart sound and its variations, as determined by this study, is shown in Figure 4.

The Q-II_A in inspiration and expiration was found to vary with heart rate , and this linear dependence of Q-II_A on the heart rate is shown in the form of scattergrams (Figures 5a, 5b).

FIGURE 3





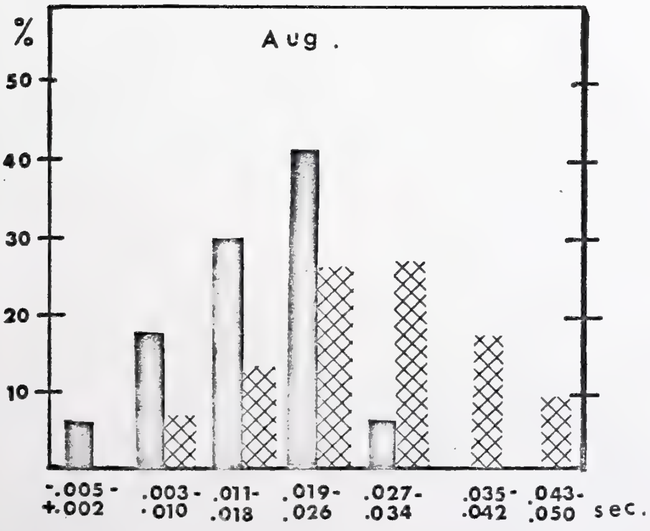


Figure 3a,b,c: Distribution curves for A_2-P_2 in inspiration and expiration and the inspiratory augmentation of A_2-P_2. Solid lines represent population with obstructive pathology; cross-hatched represent normal population. Similar distribution patterns are noted here as in Figure 2a,b.

FIGURE 4

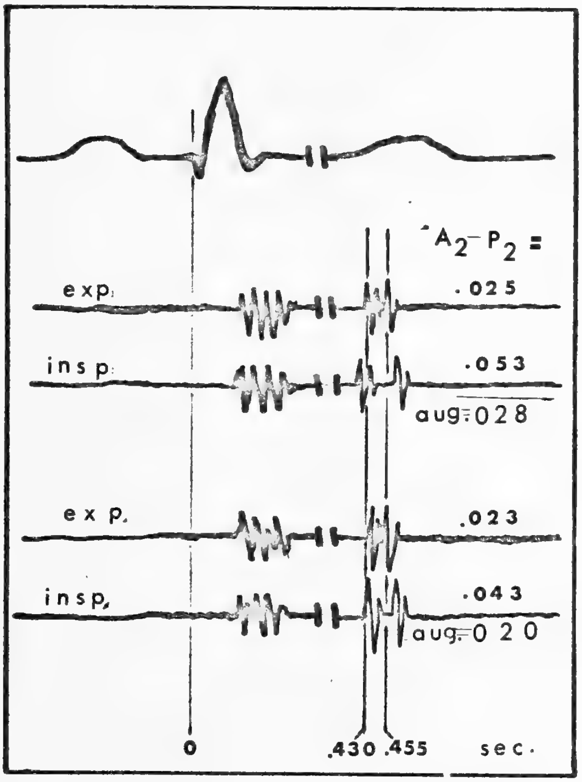


Figure 4: The second heart sound in a normal subject (first two phonocardiographic tracings) and in a patient with aortic stenosis. All numbers refer to time in seconds. Note that in the normal subject the inspiratory augmentation of the A_2-P_2 split is contributed to by the earlier arrival of the aortic component (shorter Q-II_A) as well as by the delay in arrival of the pulmonic component (longer Q-IIp). In the patient with an obstructive lesion the aortic component is relatively "fixed" in both stages of respiration. It is late in expiration. It is later still in inspiration, since it does not move to the earlier position which it normally occupies in inspiration. The aortic component's contribution to inspiratory augmentation of A_2-P_2 has been negated. The end result is a slightly narrowed expiratory split and a relatively greater narrowing of inspiratory splitting.

FIGURE 5

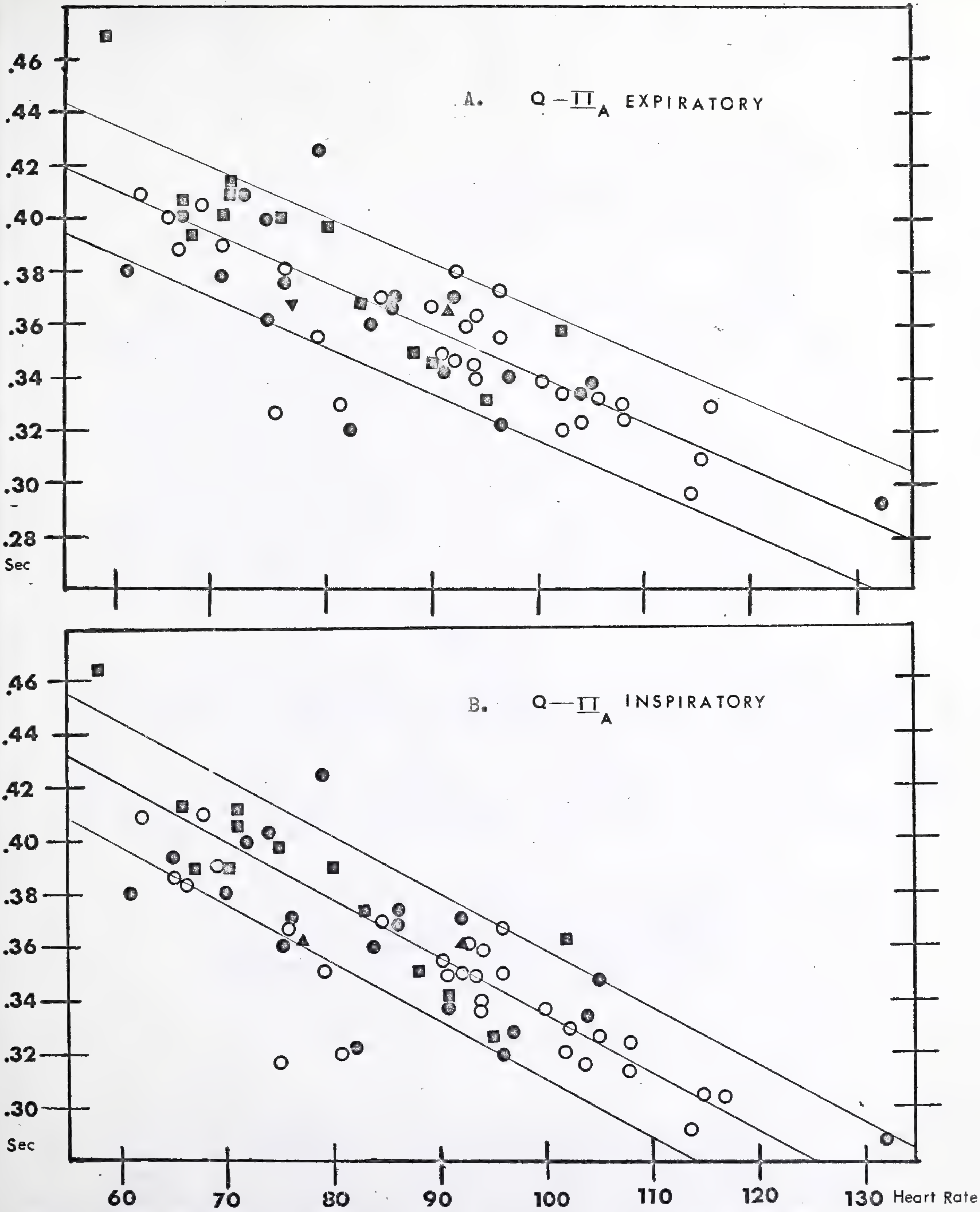


Figure 5a,b: Scattergrams representing the linear relationship between heart rate and Q-II_A in expiration and inspiration. Legend: circles--normal population; dots--patients with aortic stenosis but no angiographic data; boxes--patients with angiographic evidence of aortic stenosis; triangles--coarctation of the aorta. Heart rate is in cardiac cycles per minute.

B. Subjects with Obstruction to Left-Heart Outflow

Data were obtained in thirty-four patients with left-heart obstruction in the same manner as in the normal population. The mean values for each interval for this population are presented in Table 2. The mean expiratory Q-II_A was 0.432 seconds, which is not significantly different from the mean value (0.430 seconds) found in the normal group of subjects. The mean inspiratory Q-II_A was 0.431 seconds, which is a delay of slight significance.*

TABLE 2

Expiratory Q-II_A	Inspiratory Q-II_A	Expiratory A_2-P_2	Inspiratory A_2-P_2	In spiratory Augmentation of A_2-P_2
0.432 ± .009	0.431* ± .024	0.026 ± .014	0.043 ± .015	0.017 ± .008***

Mean values for phonocardiographic data obtained in the study of thirty-four patients with left-heart obstruction. ± indicates standard deviation. Significance is represented by * when p is less than .10 and *** when p is less than .02.

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* The term 'significance' reflects mathematical theory, not necessarily physiology. It is dependent on population size, symmetry of distribution, and variance about the mean value. This increase could be real physiologically, and therefore cannot be dismissed merely because it also could have occurred by chance--especially in view of the other significant alterations in Q-II_A as noted later in those cases diagnosed as moderately severe aortic stenosis.

The mean expiratory A_2-P_2 (0.026 seconds) is not significantly altered. The inspiratory A_2-P_2 split (0.043 seconds) is, however, significantly decreased, as is the inspiratory augmentation of split (0.017 seconds).

The distribution curves (Figures 2, 3) and scattergrams (Figure 5) representing this population are less nearly Gaussian curves. Some of them are skewed or even bimodal, suggesting a heterogeneous population composed of some subjects with values overlapping those of the normal population and others whose values tend more toward those obtained as means for the pathologic population as a whole. This becomes clearer when the above thirty-four subjects with obstructive pathology are broken down into the following five groups:

1) 19 subjects in whom the clinical diagnosis of aortic stenosis has been made. The diagnoses have not been documented by catheterization studies, since in nearly all the cases the obstruction is felt to be mild and of minimal physiologic significance;
2) 3 subjects with mild aortic stenosis as evidenced by catheterization; i.e., studies showing pressure differences of less than 30 mm. of mercury;
3) 7 subjects with moderate aortic stenosis and pressure differences of 31-60 mm. of mercury;
4) 4 subjects with severe obstructions causing pressure differences of more than 61 mm. of mercury;
5) 2 subjects with coarctation of the aorta who will be considered separately from the first four groups.

The Q-II_A and A_2-P_2 during both phases of respiration were statistically analyzed for each group and the mean values are entered in Table 3 along with their respective standard deviations and the significance levels of the deviations from the means of the normal population.

It can be seen that with increasing severity of obstruction the mean expiratory Q-II_A becomes slightly but significantly delayed. This trend can be observed in the first three groups, but it breaks down when those subjects with the most severe lesions are studied. This pattern persists throughout the study and will be investigated in the section entitled "Discussion".

The Q-II_A interval during inspiration appears to be even more influenced by the severity of the lesion than during expiration. Another way of viewing this is to note that the physiologic variation of aortic closure timing is progressively decreased, to the extent that it occurs at nearly the same time in both the inspiratory and the expiratory phases of respiration. Unlike the normal subject whose Q-II_A occurs earlier with inspiration, the obstructed patient has a Q-II_A which remains relatively fixed and uninfluenced by respiration. This alteration is demonstrated graphically in Figure 4.

The expiratory A_2-P_2 split is only slightly decreased in obstructive disease. This follows from the fact that the pulmonic component of the second sound, which is unaffected by the left-sided pathology, remains in its normal position while the expiratory Q-II_A is only slightly decreased, as mentioned above. The inspiratory A_2-P_2, in contrast, becomes progressively decreased as

SUBJECTS	$Q\text{-}II_A$ EXPIRATORY	$Q\text{-}II_A$ INSPIRATORY	$A_2 - P_2$ EXPIRATORY	$A_2 - P_2$ INSPIRATORY	INSPIRATORY AUGMENTATION OF $A_2 - P_2$
NORMAL CONTROL POPULATION	0.430 ± .012	0.422 ± .021	0.025 ± .011	0.053 ± .021	0.028 ± .010
1) CLINICAL DIAGNOSIS OF OBSTRUCTION	0.427 ± .038	0.426 ± .027	0.026 ± .016	0.046 ± .016*	0.019 ± .007***
2) MILD STENOSIS	0.441 ± .067	0.437 ± .022	0.023 ± .014	0.044 ± .010	0.021 ± .008
3) MODERATE STENOSIS	0.445 ± .071***	0.441 ± .018**	0.027 ± .013	0.036 ± .015*	0.009 ± .005***
4) SEVERE STENOSIS	0.420 ± .050	0.418 ± .038	0.020 ± .012	0.036 ± .017	0.011 ± .015***

TABLE 3. PHONOCARDIOGRAPHIC FINDINGS

LEGEND: (all values are rate-corrected)
± indicates standard deviation within population tested
* indicates a difference from the mean of the normal population with significance of p less than .10
** indicates significance of p less than .05
*** indicates significance of p less than .02

the obstruction becomes more severe. This follows from the increasingly delayed aortic component during inspiration in relation to the normally positioned pulmonic component.

The net result of these alterations in inspiratory and expiratory splitting is that the inspiratory augmentation of A_2-P_2 is also diminished in response to left-sided obstructive pathology. No cases of actual paradoxical splitting were seen in the population studied.

The two patients with coarctation of the aorta were studied. The subject with the milder lesion had a shortened Q-II_A interval in both inspiration and expiration with an approximately normal pattern of splitting of the second heart sound. The more severe coarctation revealed delayed Q-II_A intervals in both phases of respiration and, again, a roughly normal pattern of A_2-P_2 split.

The above-mentioned intervals were plotted against magnitude of pressure difference (Figure 6). Average values in the mild, moderate, and severe categories were also plotted for each variable and used to suggest slopes. Although the numbers of subjects involved in this study are too small, and the normal variations too large to attempt any definitive correlations, the tendencies in the presence of obstructive pathology which are discussed above are graphically seen. This is, the Q-II_A tends to arrive late, the splitting tends to narrow and the inspiratory augmentation of A_2-P_2 tends to diminish as lesions become more severe.

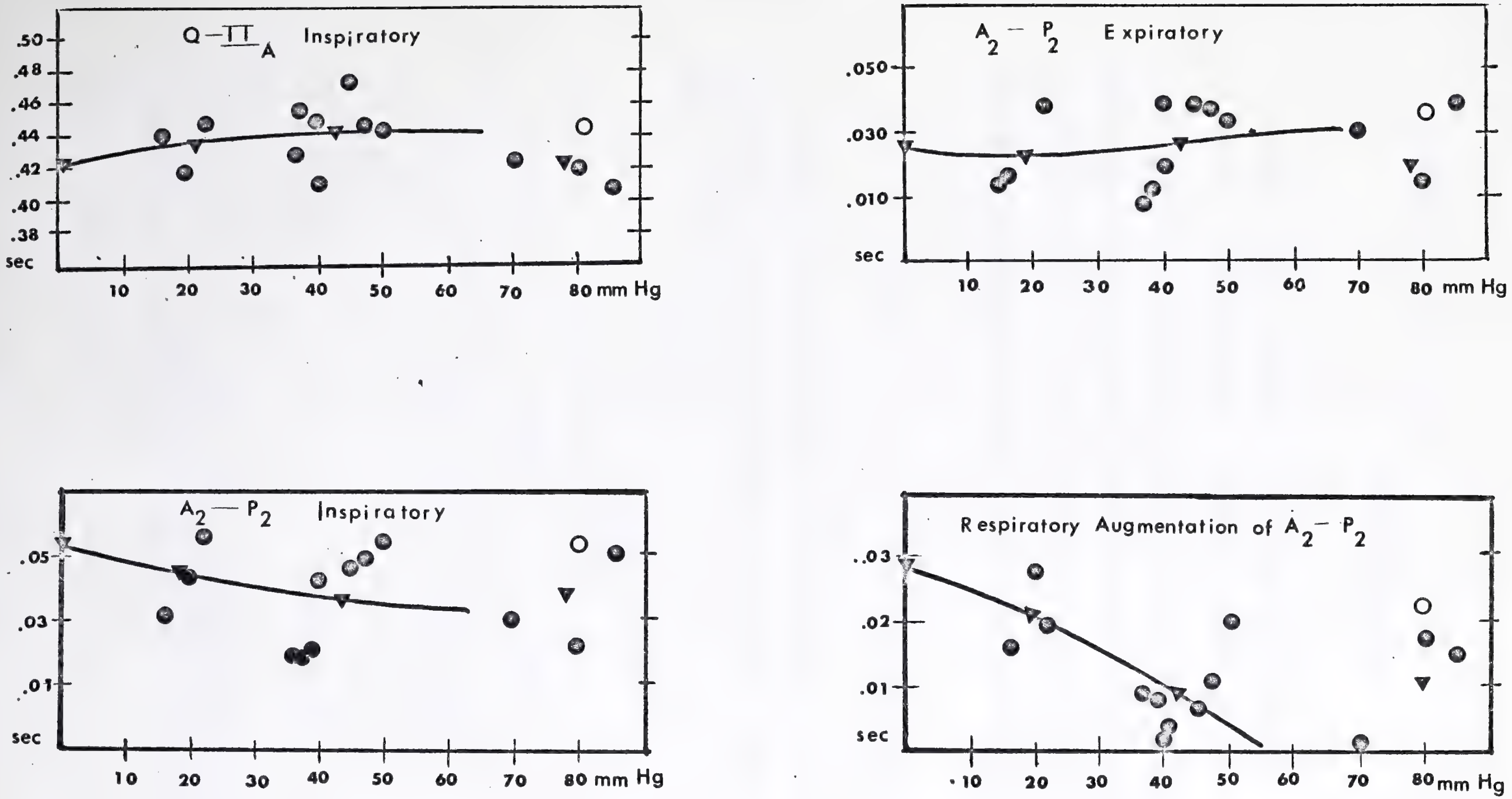


Figure 6: Scattergrams of pressure difference across obstructive lesion vs. (a) inspiratory $Q\text{-}II_A$; (b) expiratory $A_2\text{-}P_2$; (c) inspiratory $A_2\text{-}P_2$; and (d) respiratory augmentation of $A_2\text{-}P_2$. Slopes are based on mean values as determined for the normal population and the populations with mild, moderate, and severe aortic stenosis. Legend: dots--patients with aortic stenosis; circles--coarctation of the aorta; triangles--mean values for each group.

II. Carotid Tracing Studies

A. Normal Subjects

Carotid pulse tracings were measured and analyzed in a control population of thirty normal subjects. The mean total ejection time (0.322 seconds), mean upstroke time (0.090 seconds), and mean t-time (0.034 seconds) are all entered along with their standard errors and standard deviations in Table 4. Their distribution curves (shown in Figure 7) are nearly Gaussian.

B. Subjects with Left-Sided Obstructive Pathology

Thirty-three patients with clinical and/or catheterization-documented diagnoses ofobstructive lesions were analyzed for the same three intervals (Table 4).

TABLE 4

Subjects	E-time	u-time	t-time
Normal Control Population n = 30	0.322 ± .018 SE = ± .066	0.090 ± .018 SE = ± .006	0.034 ± .010 SE = ± .004
Patients with Left-Heart Obstruction n = 33	0.339* ± .022	0.093 ± .017	0.033 ± .017

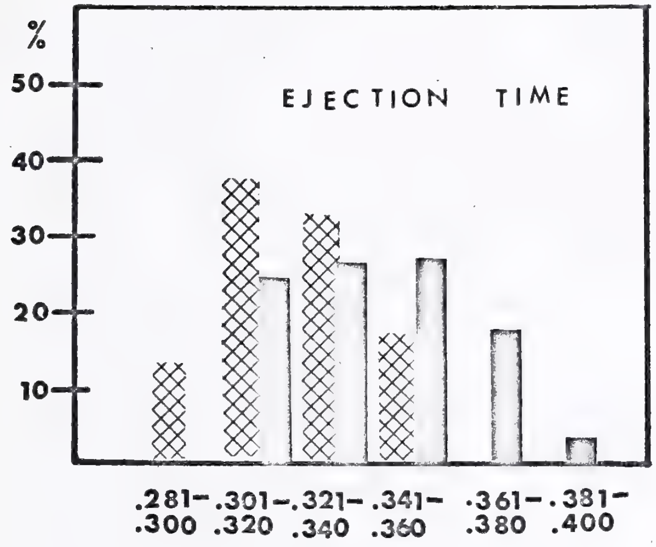
Tabulation of Carotid Pulse Data: All intervals are in seconds; ± indicates standard deviation; SE indicates standard error about the true mean; 2 x SE gives the confidence with p less than .05; * indicates significant at the p less than .05 level.

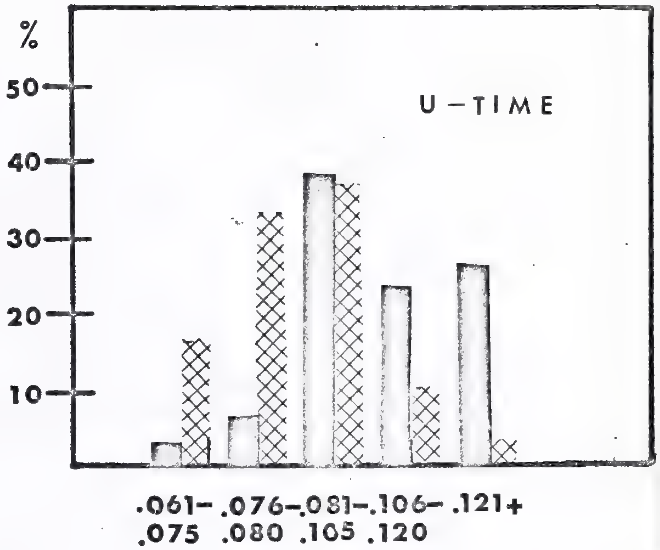
The values obtained were not significantly prolonged in the cases of the mean u-time (0.093 seconds) and the t-time (0.033 seconds), but the mean ejection time (0.339 seconds) was significantly increased over the ejection time of the control population (0.322 seconds). Among the assumptions made in determining the statistical significance is that both the control and pathologic populations constitute symmetrical Gaussian distribution curves about their mean values. As can be seen by reference to the distribution curves in Figure 7, the validity of this assumption is questionnable in the cases of the u- and t-times and only approximately correct in the distributions of the e-time. Studies of a larger population would clarify the issue. Further, a more technically accurate method is probably needed for studying these variables. The present technique utilizes an interval, the beginning of which is a somewhat ambiquous curved line without any sharply defined demarcation point.

As before, in the phonocardiographic studies, the physiologic as well as the statistical significance of these figures becomes more apparent when the entire group of subjects is again broken down into groups based on the severity of obstruction as determined by angiography (see Table 5).

By plotting ejection time against pressure difference it is apparent that the mean ejection time becomes increasingly prolonged as the pressure gradiant across the obstruction becomes increasingly more severe (see Figure 8a). As noted before in the phonocardiographic studies, this type of correlation between pressure gradiant and prolonged ejection holds true only as long as the obstruction

FIGURE 7





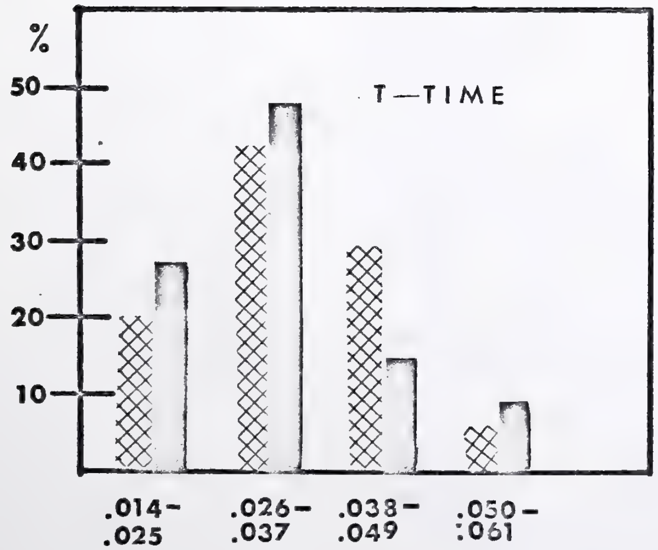


Figure 7: Distribution curves for carotid pulse wave data.

Legend: Solid bars represent population with obstructive pathology; cross-hatched bars indicate normal population.

SUBJECTS	EJECTION TIME	UPSTROKE TIME	t-TIME
NORMALS	0.322 ± .018	0.090 ± .018	0.034 ± .010
1) CLINICAL DIAGNOSIS OF OBSTRUCTION	0.335** ± .020	0.090 ± .017	0.031 ± .009
2) MILD	0.341* ± .017	0.098 ± .007	0.040 ± .065
3) MODERATE	0.362*** ± .014	0.107** ± .014	0.038 ± .012
4) SEVERE	0.334 ± .014	0.083 ± .010	0.028 ± .010

TABLE 5

Data from Carotid Pulse Tracings. All intervals in seconds. ± indicates one standard deviation. Significance levels: * -- p less than 0.10; ** -- p less than 0.05; *** -- p less than 0.02.

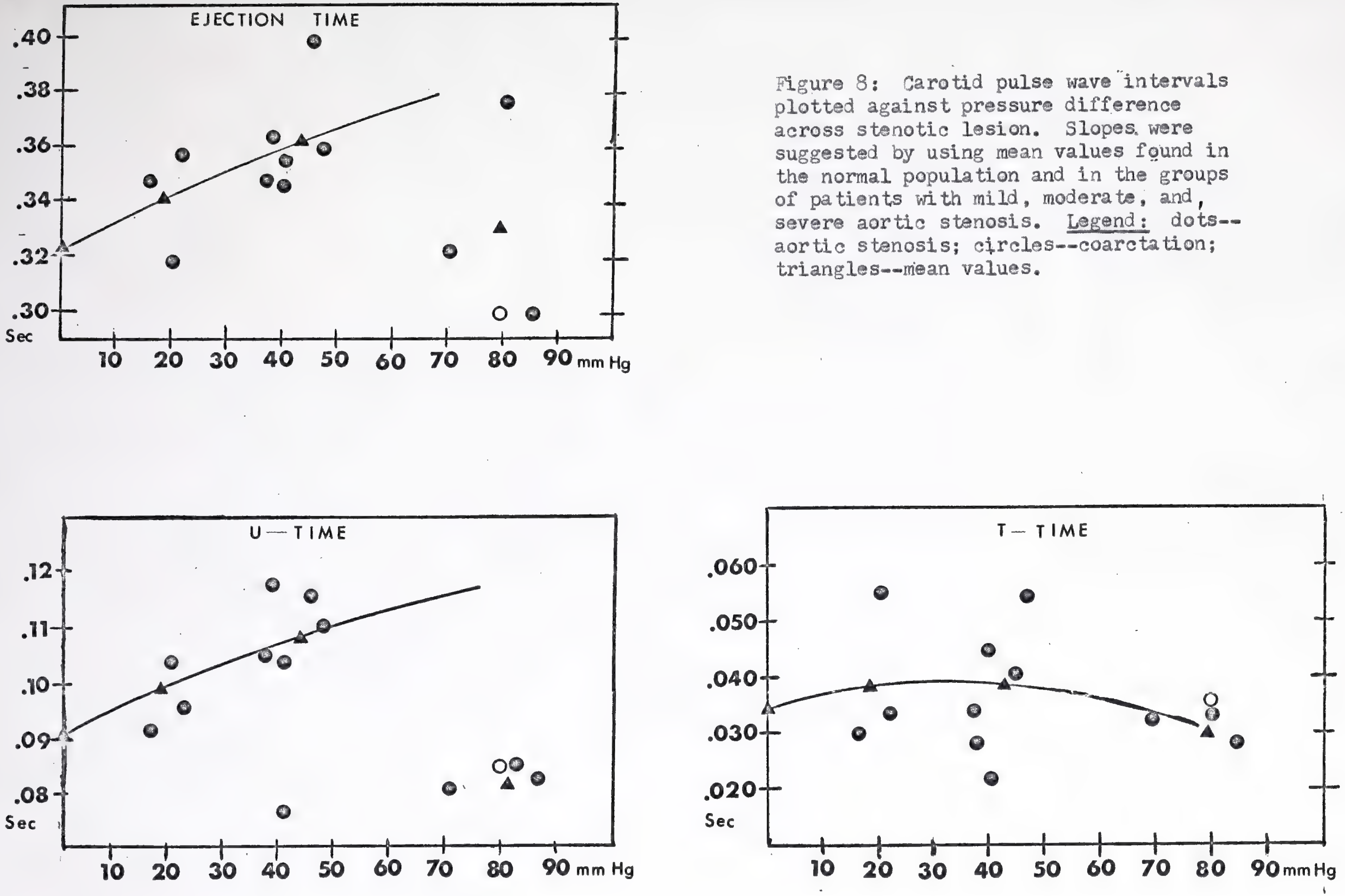


Figure 8: Carotid pulse wave intervals plotted against pressure difference across stenotic lesion. Slopes were suggested by using mean values found in the normal population and in the groups of patients with mild, moderate, and, severe aortic stenosis. Legend: dots--aortic stenosis; circles--coarctation; triangles--mean values.

FIGURE 8

is moderately severe. The most severe cases have a mean ejection time which approaches the normal value--in spite of definite pathophysiology.

The mean upstroke time follows the same trend and pattern, while the t-time becomes a somewhat erratic indicator of obstruction to systolic ejection (see Figures 8b, 8c).

Of the two subjects with coarctation of the aorta, the patient with the milder lesion had a low-normal ejection time, a quick upstroke time, and a normal t-time. The patient with severe coarctation had a low-normal ejection time, a low-normal upstroke, and a normal t-time.

DISCUSSION

Detectable splitting and respiratory variations in the timing of the aortic and pulmonic components of the second heart sound have been documented in the presence of physiologic pressure and volume loads. Patients with aortic stenosis and coarctation of the aorta were then studied. In the presence of obstruction to left ventricular ejection, a different pattern of splitting was documented. This altered pattern was shown to be due to a "fixed" delayed appearance of the aortic component. That is, the aortic component was shown to occur not only late, but in a pattern which did not demonstrate respiratory variations in timing. Further, the behavior of the aortic component was shown to be related to the degree of obstruction, although not in the direct manner which had been anticipated.

In the normal pediatric population there was detectable splitting of the second heart sound and physiologic inspiratory augmentation of this split in every subject tested. Movement of the aortic component to an earlier position was responsible for twenty-nine per cent of this inspiratory augmentation, while delay of the pulmonic component contributed the remaining seventy-one per cent. While splitting has been observed since the Nineteenth Century (Potain) and explained in terms of asynchronous ventricular systole since 1925 (Katz), the relative importance of the variation in the timing of each semi-lunar valve's closure has been

studied phonocardiographically only recently. The findings of the present study contrast with those of Leatham and Towers. These investigators felt that delay in pulmonic closure was the sole determinant of inspiratory augmentation of splitting. The present study, on the other hand, confirms the findings of Boyer and Chisolm, Shafter, Castle and Jones, Aygen and Braunwald, and Shah and Stodki, who have all shown data to support the view that earlier aortic valve closure accounts for twenty to forty per cent, and that later closure of the pulmonic valve accounts for sixty to eighty per cent of the increased duration of the A_2-P_2 interval in inspiration. (These slight differences in findings can probably be attributed to the difference in age groups studied, since it is well documented that age effects the A_2-P_2 interval. Cf. Shah and Stodki.).

The mechanism accepted by most authorities is that inspiration reduces intrathoracic pressure causing increased inflow into the right ventricle (Brecher and Hubay) and increased end diastolic volume (Boyd and Putras) as the blood pooled in the systemic venous system flows more easily into the right side of the heart. This results in increased right-sided ventricular stroke volume (Shuler et al.). The ventricle requires more time to eject the increased volume (Braunwald et al., 1958; Weissler et al., 1961), and this delays pulmonic valve closure, accounting for this valve's contribution to the augmentation. The early closure of the aortic valve in inspiration has been explained by most investigators as being due to decreased stroke volume. Lauson et al., Wiggers, 1949, Shuler et al. all believed that there was an enlarged pulmonary

vascular bed occurring during inspiration which resulted in diminished pulmonary venous return to the left side of the heart and diminished stroke volume. This explanation was challenged by some authors (Visscher, Shafter) who felt that pulmonary vasculature actually decreases in volume during inspiration. The experimental work of Domhorst et al. suggested that the heart's augmented (inspiratory) volume required a few seconds to traverse the pulmonary vascular bed. By the time the left heart received this augmented volume, several seconds had elapsed, and the expiratory stage of the respiratory cycle had been reached. Supportive evidence for this hypothesis is derived from the fact that during prolonged respiratory cycles, the wide inspiratory split becomes narrowed after a few seconds. That is, both ventricles assume more nearly equal stroke volume. Similarly, during prolonged expiration the narrowed A_2-P_2 interval widens slightly after a few seconds.

As noted above, the right and left sides of the heart have been shown to contribute unequally to the inspiratory variation in splitting of the second heart sound. That is, they respond differently to the respiratory augmentation of ventricular stroke volume, the right ventricle showing a greater prolongation of systole (Q-II_A) than does the left. This is to be expected, since the two sides of the heart are not identical and therefore do not obey Starling's Law equally well. The right ventricle is less muscular, pumps at a lower pressure, and demonstrates a greater compliance, while the left is more muscular, less compliant and pumps at a higher pressure. Experimentally, it has been shown that

the respiratory variations in ventricular volume are actually greater on the right than on the left side (Shuler et al., Dupee and Johnson, Lauson et al.). This is probably partially due to the greater compliance of the right ventricle (Moss and Johnson). Further, the pulmonary vasculature seems to act as a buffer against rapid changes in pulmonary venous return to the left heart. The net result is that during inspiration, the right heart is capable of receiving and pumping a larger volume load, but requires extra time in systole to eject the extra volume load. The left heart during expiration, on the other hand, receives a less variable load from the lungs, is less capable of altering ventricular volume, and alters the duration of left ventricular systole relatively less in response to an augmented volume load. All this is reflected by the fact that the right heart contributes to a greater degree than the left ventricle to respiratory variations in splitting of the second heart sound.

In contrast to the normal physiology described above, left-sided obstruction produces an altered pattern of second heart sound splitting. The pattern has been characterized clinically as narrowed, single or paradoxical, depending on the relationship existing between the aortic and pulmonic components. The exact nature of narrowed splitting is not apparent, however, clinically. In pulmonic stenosis, the clinician observes that the pulmonic component follows the aortic component by a larger than normal but physiologically varying interval. Since the aortic component is a relatively stable temporal reference point, lying in close proximity to the pulmonic component, this pathologic alteration

is easily appreciated by the ear. Phonocardiographic studies have amply documented the mechanism of the wide splitting heard in the presence of pulmonic stenosis by showing prolonged Q-IIp and A_2-P_2 intervals (Vogelpoel and Shrire, Leatham and Weitzman, Gamboa). In aortic stenosis, on the other hand, there has been more difficulty both in the clinical appreciation and in the phonocardiographic documentation of the pathologic alteration in the second heart sound. Clinically, the ear has only two reference points, neither of which serves very well. The first heart sound is temporally quite remote, somewhat variable, and occasionally difficult to hear at the pulmonic area where the second heart sound is being studied. The pulmonic component varies too greatly with respiration in children and may be difficult to hear in adults. Further, the pulmonic component may be obscured by the simultaneous occurrence of the louder aortic component. Of course, the Q-wave which was used as the reference point in this study is completely undetectable to the clinician, although it serves as a very reliable reference point in phonocardiographic studies.

Since all that could be detectable clinically in left-sided obstruction was a narrowed splitting of the second heart sound with the aortic component in close relation to the pulmonic, the explanation was proposed that the aortic component was delayed sufficiently to approach the pulmonic component in time. Reasoning by analogy to pulmonic stenosis, where it had been shown that both delay in pulmonic closure and increased magnitude of splitting correlated to the degree of obstruction (Vogelpoel and Shrire, Leatham and Weitzman, Gamboa), various investigators (Gamboa,

Aygen and Braunwald, and Braunwald, Roberts, et al.) have sought to explain the second heart sound heard in aortic stenosis in a similar fashion. That is, they attempted to correlate delayed aortic valve closure with degree of obstruction. Aygen was able to show a prolongation of $Q\text{-}II_A$ (Aygen and Braunwald, and Aygen in Braunwald, Roberts, et al.) but was unable to demonstrate any direct numerical correlation. He was able to state only approximate limits of abnormal splitting which indicated the likelihood of certain degrees of stenosis. Patients were found, however, with very severe obstructions in the presence of normal splitting, and with normal outflow in the presence of abnormally narrow splitting.

Similar difficulties obtained in this study. No numerical correlations could be made between magnitude of $Q\text{-}II_A$ and degree of obstruction. The data were analyzed further in an attempt to make predictive statements about the degree of stenosis based on phonocardiographic measurements. Using the mean values obtained in the normal population as criteria, it was found that only seventy-two per cent of the population with documented stenotic lesions would show prolonged inspiratory or expiratory $Q\text{-}II_A$ intervals. Using the $A_2\text{-}P_2$ intervals yielded little more valuable information. However, when inspiratory augmentation of the $A_2\text{-}P_2$ interval was analyzed, it was found that all cases of documented aortic stenosis had $A_2\text{-}P_2$ inspiratory augmentation which was less than the mean normal value of 0.028 seconds.

It was therefore felt by the present investigator that a prolonged $Q\text{-}II_A$ interval did not represent an adequate explanation of the basic pathophysiology of obstruction to left ventricular

outflow. If the prolonged Q-II_A interval was the sole determinant of narrowing or paradoxical splitting, then the study should have revealed inspiratory and expiratory Q-II_A intervals which were equal to the mean values for the normal population plus a constant mean increment. The A_2-P_2 intervals in both phases of respiration should have been narrowed by that same increment. The mean inspiratory augmentation of A_2-P_2, however, should have been similar to that found in the normal group of subjects.

This study, on the other hand, revealed not only that the Q-II_A intervals are mildly prolonged during expiration (as noted in the previous studies mentioned above), but that they are relatively "fixed" at approximately the same magnitude during inspiration. Thus, during inspiration the aortic component does not move to an earlier position in the usual manner as seen in normal subjects, and as a result the aortic component is relatively later in inspiration than in expiration. Obstruction to left ventricular outflow has not only narrowed the second heart sound by moving the aortic component nearer to the pulmonic component throughout the respiratory cycle, but it has also negated the aortic component's contribution to the respiratory variation of splitting. In terms of the variables studied, the mean expiratory Q-II_A was shown to be minimally prolonged, and the mean inspiratory Q-II_A was more greatly prolonged in comparison to the same variables obtained for the normal subjects. The mean expiratory A_2-P_2 interval was normal or slightly narrowed, while the mean inspiratory A_2-P_2 interval was perceptibly narrowed. The net result, the decreased inspiratory augmentation of the A_2-P_2 split, reflected both the

prolonged systole and the altered behavior with respect to respiration. Thus, this study documented that it is more the <u>lack of physiologic variation</u> in timing, rather than the <u>absolute delay</u> of the aortic component which is responsible for the narrowed second heart sound in the presence of left-sided obstruction.

An explanation for this phenomenon may be possible. It was noted above that the right ventricle contributes more to inspiratory augmentation of the A_2-P_2 interval than does the left ventricle. In explaining this phenomenon Luisada, 1965, Castle and Jones, and Moss and Johnson place emphasis upon the differences in musculature and compliance of the right and left ventricles. They note that the duration of ventricular systole is prolonged in response to increased volume or pressure overload, but that this effect is much greater for the weaker, right ventricle than for the stronger, left ventricle. The stronger ventricle is able to respond to a greater amount of blood <u>without</u> greatly prolonging ejection time. By analogy, these statements may be applicable to the normal left ventricle and the left ventricle which is slightly hypertrophied in response to the systolic overload created by obstruction.* If the analogy holds true, then a pathologically hypertrophic obstructed ventricle should be able to handle the trivial fluctuations of volume load which occur in response to respiration without prolonging the Q-II_A interval better than

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* Braunwald, Roberts, et al. have documented the ubiquitous presence of left ventricular hypertrophy in patients with aortic stenosis.

the normal left ventricle which is somewhat weaker and which responds to the respiratory variations in blood volume by prolonging ejection.

Similar reasoning may be used to explain why the more severely obstructive lesions did not follow the general trend towards increasingly prolonged Q-II_A intervals (see Figure 6). It is reasonable to assume that these left ventricles would be more hypertrophic and better able to handle the increased pressure load without prolonation of ejection, than would be those ventricles subjected to lesser diastolic pressure loads. While other authors do not remark on this phenomenon, it is interesting to note that this might be related to the age groups chosen for study. The mean age of the population of subjects with severe stenosis presented in this study is quite young--approximately ten years of age--and presumably possessing myocardial tissue capable of compensating for the increased load better than the subjects in Aygen's or Braunwald's studies who were much older.

As stated earlier, the Q-II_A actually represents the sum of three intervals: 1) ventricular depolarization; 2) isometric contraction; and, 3) ejection time. It is generally accepted that in the absence of conduction disturbances or myocardial disease the first two intervals represent a fairly constant and small fraction of the total duration of systole, i.e., Q-II_A. If uncomplicated aortic stenosis is a purely mechanical lesion, then it should affect only the latter interval--the ejection time (as determined by the carotid pulse wave in this study). This was in fact true as evidenced by the similar tendencies shown in

both the phonocardiographic and pulsè wave studies. Both studies documented prolongation of systole in response to mild and moderate stenosis, and a general tendency towards normal values in severe stenosis.

As was shown in the literature, however, this parameter offers little ability to predict accurately the degree of severity of obstructive lesions (Benchimol and Dimond, Braunwald et al., 1963, Daoud et al., Donoso et al., Duchosal et al., Eggink et al., Epstein and Coulshed, Robinson). Only sixty-seven per cent of those subjects with documented lesions had above average ejection times. The u- and t-times were even poorer indicators of obstruction. The technique also proved inadequate in the cases of severe obstruction; the reasons for this are probably the same as those cited in the discussion of the phonocardiographic results.

It was possible to study only two patients with coarctation of the aorta, a number too small to warrant generalizations. It is, however, worthwhile to attempt to interpret their findings, especially since the hemodynamics involved are somewhat similar to those of systemic hypertension. It was noted that the subject with the milder lesion had a shortened ejection time and $Q\text{-}II_A$ interval during both expiration and inspiration. This is compatible with the earlier expierments of Wiggers (1952) in which he demonstrated slightly shortened left ventricular systole in the presence of acute aortic occlusions, and with the work of Wallace et al. who found that elevating mean aortic pressure shortened ejection time slightly more than it prolonged isovolumetric

contraction time, resulting in a slightly decreased duration of total systole. Weissler et al. (1961) found slightly shortened ejection times in patients with uncomplicated hypertension. Since ejection time, as determined at the carotid artery, is based upon the opening and closing of the aortic valve, the mechanism of prolonged ejection may be related to the higher pressure in the aorta, which must be attained by the left ventricle before the valve will open, and maintained by the ventricle if the valve is to be kept open. The patient with the severe coarctation of the aorta was discovered to have slightly prolonged $Q\text{-}II_A$ intervals in the face of abbreviated ejection times. A possible explanation here (in the absence of conduction defects) is that the isovolumetric contraction period was greatly prolonged. It is likely that it takes longer in the presence of severe coarctation for the ventricle to achieve sufficient pressure to open the aortic valve. In both cases, the degree of collateral run-off is a large but unknown factor which cannot be determined by these techniques.

CONCLUSIONS

A study of thirty normal subjects and thirty-four patients with coarctation of the aorta or discrete aortic stenosis was undertaken. The normal subjects ranged from five to fifteen years of age, and the patients with left-sided obstruction ranged from five to twenty-one years of age. Fourteen of the latter patients had angiographic documentation of their lesions.

Phonocardiographic and indirect carotid pulse wave techniques were utilized to investigate the prolongation of ejection time, the total systole ($Q\text{-}II_A$), and the resultant alterations of the behavior of the aortic and pulmonic components of the second heart sound.

A general tendency for the mechanical ejection time and upstroke time to be increased was found when patients with obstruction were compared with the normal population. The t-time proved to be of little value in distinguishing patients with obstruction from the normal population. No direct correlation could be found, however, between degree of obstruction and prolongation of ejection and upstroke times. The major reasons for the lack of correlation were felt to be the large normal variation and the small number of subjects studied. It is unlikely that increasing the population size would increase the value of this technique as a diagnostic tool, since the overlap between the normal and disease populations was substantial. The value of this technique as a diagnostic tool, therefore, is limited.

Phonocardiographic studies of the aortic and pulmonic components documented altered hemodynamics in the presence of obstruction to left ventricular outflow. In the normal population it was found that the inspiratory augmentation of the splitting of the second heart sound was contributed to by two unequal factors; namely, the prolongation of $Q\text{-}II_P$, which was the major factor, and the shortening of $Q\text{-}II_A$, which was the lesser factor. In contrast to these findings, left-sided obstruction in the pediatric population was shown to produce a narrowed second heart sound due to the prolongation of $Q\text{-}II_A$ and due to the lack of variation in the left ventricle's $Q\text{-}II_A$ interval in response to the phases of respiration. It was shown that the magnitude of the respiratory variation of the $A_2\text{-}P_2$ interval represents a better measure of left ventricular obstruction than does the $Q\text{-}II_A$ interval or $A_2\text{-}P_2$ interval which has been used in the literature.

An attempt was made to explain these alterations of the components of the second heart sounds in terms of normal and pathological volume and pressure loads, and the responsiveness to these loads on the part of right, left, and pathologically hypertrophied left ventricles.

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